Optoelectric scaffold for photo-responsive biological components.

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Fig. 1A

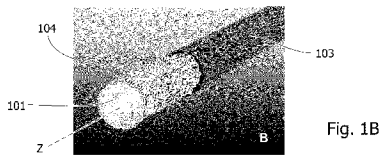

Fig. 1B

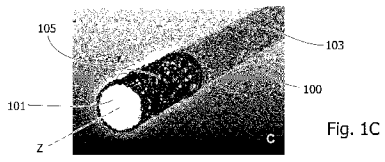

Fig. 1C

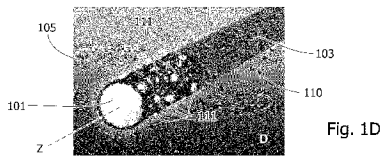

Fig. 1D

(57) Abstract: According to one aspect, an optoelectric scaffold for accommodating photo- responsive biological components is provided. The scaffold comprises an optical waveguide configured for confining light propagating in a longitudinal direction thereof. The optical waveguide comprises at least one leaky section with enhanced emission of light in a direction transverse or lateral to the longitudinal direction. The scaffold further comprises an electrically conductive layer arranged on an outer surface of the optical waveguide, wherein the electrically conductive layer has an immobilisation or growth support surface for the immobilisation or cultivation of photo-responsive biological components thereon. The electrically conductive layer comprises transparent regions at least partially overlapping the leaky section. The transparent region is configured so as to transmit light from the leaky section of the waveguide to the immobilisation and/or growth support surface. According to a further aspect, an optoelectric device comprises an optoelectric scaffold and a photo-responsive biological component arranged on the immobilisation/growth support surface. The growth support surface is arranged so as to transmit light received from the leaky section of the optical waveguide to the biological component placed thereon.

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Optoelectric Scaffold for Photo-Responsive Biological Components

FIELD

An optoelectric scaffold holding photo-responsive biological components and a method of producing the optoelectric scaffold are provided.

BACKGROUND

Recent developments in the field of carbon electrode technologies in the microscale have shown that microscale conductive carbon electrodes are particularly useful as scaffolds for cultivating biological cells thereon and at the same time perform electrochemical experiments on the cells, e.g. for detecting and monitoring biological activity. For example, recent studies show that microscale patterned conductive carbon electrodes made of pyrolysed SU-8 photoresist can be used to promote differentiation of human neural stem cells towards dopaminergic cells and monitor the stimulated release of dopamine, see e.g. Amato et al. (2014) “Pyrolysed 3D-Carbon Scaffolds Induce Spontaneous Differentiation of Human Neural Stem Cells and Facilitate Real-Time Dopamine Detection”, Adv. Funct. Mater., 24: 7042–7052.

SUMMARY

It is an important merit of the optoelectric scaffold disclosed below that recent achievements in the field of microscale conductive electrodes have been developed further for use in combination with photo-responsive biological components in order to synergistically facilitate the practical application of photo-responsive biological components.

Indeed, numerous efforts have been made to harness photo-responsive biological components for a large range of applications spanning as wide as from medical applications to energy applications.

However, one challenge in this context is providing a viable concept for the infrastructure combining in one device a viable support for immobilising or cultivating the biological components to be harnessed as well as optical access and good electrical contact to the immobilised or cultivated biological components.

Therefore, it is an object of the present invention to provide a viable concept that may easily be adapted to provide the necessary infrastructure for the practical application of photo-responsive biological components within fields of application as different from each other as medical applications and energy applications.

According to a first aspect, the object is fulfilled by an optoelectric scaffold for accommodating photo-responsive biological components, wherein the scaffold comprises an optical waveguide configured for confining light propagating in a longitudinal direction thereof. The optical waveguide comprises at least one leaky section configured for enhanced emission of light in a direction transverse or lateral to the longitudinal direction of the optical waveguide. The optical waveguide further comprises an electrically conductive layer arranged on an outer surface of the optical waveguide. The electrically conductive layer has a support surface for accommodating the photo-responsive biological components and transparent regions at least partially overlapping the at least one leaky section for transmission of light to biological components when accommodated at the support surface.

The electrically conductive layer should be made of a material that provides a biocompatible support surface. Biocompatibility is here to be understood as compatibility with respect to the photo-responsive biological components for which the optical scaffold is designed. The term ‘biocompatible’ thus refers to the quality of not having toxic or injurious effects on the biological elements/components/systems in question.

Within the context of the present application, the terms “optical” and “light”, without any further specification, relate to electromagnetic radiation including the UV, visible and infrared regions, in particular near infrared. The terms “optical” and “light” may thus refer to wavelengths in the range above 100 nm, above 200 nm, above 300 nm and up to 1 µm, up to 2 µm or up to 3 µm, wherein the visible range of the spectrum in agreement with common definitions is considered to range from about 400 nm to about 700 nm. The term “photo” denotes phenomena related to the conversion of light with a certain spectral specificity, i.e. occurring within a relevant spectral range as determined by the respective phenomenon.

Throughout the present disclosure, the term “biological component” denotes one or more biological cells of one or more types of biological cells; or, one or more parts of biological cells.

Biological cells include single celled or multicellular living organisms, such as microorganisms, mammalian cells, e.g. mesenchymal stem cells, or neural stem cells, or other cells capable of, possibly having been modified to be capable of, producing and releasing a substance beneficial for the treatment of a disease, etc.

Parts of biological cells include enzymes, proteins, membranes, such as thylakoid membranes, etc., organelles, such as chloroplasts, etc., etc.

A photo-responsive biological component is a biological component that provides a response to light incident upon it.

A scaffold for accommodating photo-responsive biological components is hereby provided that yields both optical and electrical access to the biological components. In particular, an optoelectrical configuration is provided, where photo-responsive biological components accommodated at the support surface of the scaffold, can be illuminated from the side facing the optical waveguide, and at the same time can be contacted electrically via the conductive layer making up the support. Simultaneously, the biological components accommodated at the support surface can be exposed to a predefined environment, e.g. in an electrochemical set-up, if desired.

Regarding the term “enhanced”, the emission of light in a direction transverse or lateral to the longitudinal direction within each of the at least one leaky section, in the following denoted “leaky emission”, is enhanced as compared e.g. to remaining “non-leaky” sections of the optical waveguide. Alternatively or in addition thereto, the leaky emission from the optical waveguide may be enhanced within a given spectral region for leaky emission (one or more leaky bands) as compared to the transverse or lateral loss of light for waveguide modes in spectral ranges outside the given spectral region for leaky emission. The electrically conductive layer comprises one or more transparent regions at least partially overlapping the at least one leaky

section both spatially and spectrally, thereby allowing for the transmission of light that is coupled into the optical waveguide for propagation in the longitudinal direction, that is leaked at the at least one leaky section in transverse or lateral directions through the one or more transparent regions to photo-responsive biological components accommodated at the support surface.

Advantageously according to some embodiments, the electrically conductive layer may be a conductive carbon layer, e.g. a layer made by pyrolysing a layer of polymer resulting in a layer of pyrolytic carbon; a layer of a conducting polymer; a layer of a polymer made conductive by inclusion of conductive nanoparticles, such as carbon nanoparticles, etc.; a layer including graphene, etc.; As further detailed below, a conductive carbon layer has advantages with respect to its generally good biocompatibility, and with respect to producing micro-structured regions that at the same time provide a support surface for the biological components, optical access through the layer for illuminating the biological components “from behind”, and an efficient collection of any photo-induced electrical response.

Advantageously according to some embodiments the leaky emission of light in transverse or lateral directions of the optical waveguide is achieved e.g. by so-called “leaky modes” which have an enhanced emission in transverse or lateral directions as compared to guided or confined modes. Alternatively, or additionally, leaky emission in the at least one leaky section may be provided by partial or complete removal of the cladding, internal modification of the waveguide properties, roughening of the waveguide surface, e.g. by etching, etc., etc. Furthermore, the at least one leaky section provides enhanced emission in transverse or lateral directions at least within a first spectral band. Accordingly, the transparent region of the electrically conductive layer must be transparent at least for sub-bands within the one or more spectral bands with leaky emission in order to allow for transfer of light to the support surface and further to any photo-responsive biological components thereon. Furthermore, the spectral characteristics of the delivered light needs to allow for stimulating the desired photo-response of the photo-responsive biological components. Preferably, the spectral characteristics of the at least one leaky section and the spectral characteristics of the transparency of the transparent regions of the electrically conductive layer and the spectral characteristics of the

photo-response of the biological components are matched such that respective sub-bands of enhanced leakage, transparency, and photo-response at least overlap. Preferably, these spectral characteristics are matched to optimize the photo-response with respect to the light input. Optimizing criteria may depend on the respective application and can be derived accordingly. For example, in a power conversion application intended for converting input light power into electrical energy an optimizing criterion may be derived as maximizing the electrical energy output with respect to the light input power by maximizing the integrated spectral overlap of the leaked light power, of the transmission through the electrically conductive layer, and of the release of electrons from a given photo-responsive biological component for photoelectric conversion. To give another non-limiting example, optimization criteria may be set up for adapting the spectral characteristics of a light signal delivered at the support surface to maximize its overlap with spectral characteristics for the photo-responsive release by the cultivated biological component of a substance beneficial for the treatment of a disease.

Light is coupled into the optical waveguide at one end and propagates along the optical waveguide to a leaky section of the at least one leaky section. In each leaky section of the at least one leaky section, light is emitted in directions transverse or lateral to the longitudinal direction of the waveguide and reaches the electrically conductive layer. The electrically conductive layer is arranged on the outside of the waveguide, at least partially covering the at least one leaky section. The electrically conductive layer has an inwardly facing interface with the optical waveguide oriented towards the waveguide, and an exposed surface facing away towards the surroundings. The exposed surface is adapted to accommodate the biological components and for example act as immobilisation or growth support surface for the biological components. The electrically conductive layer comprises transparent regions overlapping one or more or all leaky sections of the at least one leaky section. The electrically conductive layer may in itself be transparent to light at least within one or more relevant spectral sub-bands of the light. Alternatively or in addition thereto, the transparent regions may be formed by a thinning of the electrically conductive layer, by a perforation of the electrically conductive layer and or by a nano- and/or microscale structuring of the electrically conductive layer. The term “transparent” should be interpreted as allowing a substantial portion of light

within a given wavelength band entering the leaky section to propagate through a transparent region of the transparent regions from the leaky section in question in a direction lateral or transversal to the direction of propagation of the light at entry to the leaky section in question.

At least 5%, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%, of light in the wavelength band entering the at least one leaky section is transmitted through the transparent regions of the electrically conductive layer from the at least one leaky section in a direction lateral or transversal to the direction of propagation of the light at entry to the leaky section in question. The light emitted from the one or more or all leaky sections of the at least one leaky section and transmitted through the transparent regions of the electrically conductive layer can then finally couple to photo-responsive biological components accommodated, e.g. immobilised or cultivated, at the exposed surface of the electrically conductive layer.

The exposed surface delimits the electrically conductive layer material and thereby defines an interface of the electrically conductive layer opposite to the interface of the electrically conductive layer with the optical waveguide. The exposed surface may have any suitable form. To provide some non-limiting examples, the exposed surface may be smooth, it may define a uniform layer thickness of the electrically conductive layer with respect to the interface with the optical waveguide, it may be patterned with a two-dimensional nano- and/or microscale pattern, it may be porous, it may comprise quasi three-dimensional structures, e.g. pillars projecting outwardly with respect to the optical waveguide, it may be formed by a truly three dimensional microscale structure including multiple levels, it may be a microscale foam-like structure, e.g. of the open cell type, or it may be a suitable combination thereof.

A quasi three-dimensional micro-structuring of the support surface can be advantageous e.g. for an improved cultivation of cells and/or an improved electrical interaction of the biological components, and/or any substance released therefrom, with the electrically conductive layer for collecting electrical signal and/or power. A particularly improved enhancement of these effects is conceived for truly three-dimensional microstructures including vertical structures that are laterally

interconnected at different levels, thereby defining truly three-dimensional multi-level structures. In a cylindrical geometry of e.g. an optical fibre, vertical can be mapped to radial coordinates, whereas lateral directions can be mapped to angular and circumferential and axial directions, wherein axial directions are parallel to the longitudinal axis of the optical fibre. In a planar geometry waveguide, a vertical direction is to be understood as perpendicular to a plane defined by the waveguide, whereas lateral directions are to be understood as perpendicular to the vertical direction, i.e. parallel to said waveguide plane. A three-dimensional micro-structuring may also be useful for a differentiation into specific cell types, such as cells adapted for the release of a particular neurotransmitter, such as dopamine. A two- or three-dimensional micro-structuring and/or patterning may also be conceived for improving the optical coupling and transfer of light from the optical waveguide to biological components accommodated, e.g. immobilised or grown, on the exposed surface of the electrically conductive layer.

The optical configuration allows for delivering and coupling light through the optical waveguide to the photo-responsive biological component; the electrical configuration allows for collecting electrical signals and/or electrical power from the biological components provided in response to light, and allows for electrical stimulation of the biological components, e.g. for stimulation of growth and/or cell differentiation; and the configuration of the support surface as an exposed surface allows for bringing biological components, e.g. immobilised or cultivated thereon, in contact with a desired biochemical and/or electrochemical environment.

Further according to one embodiment of the optoelectric scaffold, the electrically conductive layer is a conductive carbon layer in the form of a pyrolysed polymer film. Thereby, a conductive carbon layer can be fabricated in a reliable and cost-effective manner, which in addition is particularly useful and advantageous for growing cells thereon, for performing electrochemical measurements and/or for using the optoelectric scaffold as part of an electrode in an electrochemical system.

Furthermore it has surprisingly turned out that optical fibres coated with a conductive carbon layer made of a pyrolysed polymer film remain surprisingly flexible without damaging the integrity of the electrically conductive layer and apparently without

affecting the favourable conductive properties of the electrically conductive carbon layer obtained by pyrolysing the polymer film.

The polymer may be a natural or a synthetic polymer, and advantageously, the polymer is a radiation-sensitive resist, such as a SU-8-based resist.

Further advantageously, the polymer film, e.g. a photoresist, may be patterned prior to pyrolysis so as to define a microscale structuring and/or texturing of the electrically conductive layer. Most preferably, the radiation sensitive resist is adapted for patterning by optical pattern transfer techniques, such as photolithography or mask-less optical pattern transfer techniques.

Further advantageously, the microscale structuring may be a three-dimensional structure enhancing and/or favouring the cultivation and/or differentiation of stem cells. Thereby an improved specific adaption of the photo-responsive biological component to a specific application, such as tailoring the photo-response of the biological component towards the (enhanced) release of a specific substance, may be achieved. Furthermore, an enhanced collection of electrical signals for monitoring cell activity, such as monitoring dopamine release may be achieved.

Further according to one embodiment of the optoelectric scaffold the electrically conductive layer may have a thickness ranging from 200 nm to 10 µm. An increased thickness of the electrically conductive layer may improve the conductivity of the electrically conductive layer, while a reduced thickness may facilitate formation of the transparent regions. Accordingly, the skilled person is instructed to strike a balance of transparency and conductivity when selecting the thickness of the conductive electrically conductive layer, wherein the above cited lower and upper limits of the electrically conductive layer thickness are conceived to provide an advantageous or at least useful regime.

Advantageously according to some embodiments a compromise of transparency and conductivity may be obtained by selectively thinning the electrically conductive layer only within leaky sections of the waveguide. Alternatively or in addition thereto, transparency may be enhanced by a microscale structuring of the electrically

conductive layer comprising openings (or thinned regions) arranged in a pattern that favours electrical conduction in an axial direction parallel to the longitudinal axis of the optical waveguide, and/or a nanoscale patterning that provides for an enhanced transmission of light in transverse or lateral directions while otherwise maintaining a material thickness sufficient for the required electrical conductivity. Also here, such microscale and/or nanoscale patterning may be restrained to the leaky sections of the optical waveguide and to favour electrical conductivity of the electrically conductive layer in the remaining regions.

The optical waveguide may comprise photonic crystals. Thereby, an increased flexibility of design is achieved for adapting the optical waveguide to particular applications. In particular, the leaky sections may be tailored and engineered more flexibly with respect to their optical characteristics, such as with respect to their spectral characteristics.

The optical waveguide may be a photonic crystal waveguide.

The optical waveguide may be an optical fibre. Optical fibres allow for a relatively cheap and easy fabrication of the waveguide. Optical fibres are particularly useful e.g. for applications where only a very narrow access channel is available and/or where large mechanical flexibility is required for both the optical and electrical access path. As further detailed below, embodiments using an optical fibre as optical waveguide are therefore conceived as particularly useful as part of an implantable device. As mentioned above, an optoelectrical scaffold that is surprisingly robust with respect to bending is obtained by the combination of an optical fibre coated with a pyrolysed polymer film forming the electrically conductive carbon layer.

However, embodiments of the optoelectric scaffold using an optical fibre may also be particularly useful and advantageous for other applications, such as power conversion applications, since a bundled arrangement of many optical fibre-based optoelectrical scaffolds in parallel can provide large interfacial areas for instance for cultivating microbial cultures of photo-sensitive microorganisms, for illuminating these microbial cultures from one side and yet provide a large interfacial area for

contacting an environment, such as an electrochemical environment of a bio-photovoltaic fuel cell. Embodiments of the optoelectric scaffold based on optical fibres as optical waveguide are therefore also highly scalable.

The optical waveguide may be a photonic crystal fibre.

According to a second aspect, the object of the invention is fulfilled by an optoelectric device comprising an optoelectric scaffold according to any of the above embodiments, the device further comprising photo-responsive biological components accommodated, e.g. immobilised or cultivated, at the support surface, wherein the photo-responsive biological components are in electrical contact with the electrically conductive layer, and wherein the photo-responsive biological components are arranged to receive light from the optical waveguide at the at least one leaky section, through the transparent regions of the electrically conductive layer material.

According to some embodiments of an optoelectric device for bio-photonic applications, the optoelectric scaffold carries biological components at the support surface, wherein the biological components are in optical communication with the leaky section of the optical fibre as described above, and wherein the biological components are in electrical communication with the electrically conductive layer as also described above.

A non-limiting example of photo-responsive biological components are biological components that are responsive to light, such as opto-genetically modified dopaminergic human neural stem cells that are adapted to release dopamine upon illumination with light, wherein the exocytosis of dopamine can be monitored as an electrochemical signal using the electrically conductive layer as an electrode.

Another non-limiting example of photo-responsive biological components are biological components that are responsive to light, e.g. for converting light into electrical energy, such as photo-synthetically active microorganisms like cyanobacteria or algae, or components of these such as thylakoid membranes or chloroplasts from plant cells.

In any case, as also mentioned above, the spectral characteristics of light having propagated through the optical waveguide and transparent regions of the electrically conductive layer is preferably adapted or matched to the spectral response of the photo-sensitive biological components in order to maximize their response.

Further according to one embodiment of the optoelectric device, the photo-responsive biological components are adapted for the photo-stimulated release of a substance beneficial for the treatment of a disease. Thereby a device is provided that is useful for performing an optically controlled release of the beneficial substance from the biological component for therapeutic applications. Accordingly, the release of the beneficial substance can be stimulated by light coupled into the optical waveguide.

Further according to one embodiment of the optoelectric device the photo-responsive biological components are stem cells, such as human stem cells, such as human mesenchymal stem cells, human neural stem cells, etc. Stem cells may be differentiated and adapted for the release of certain beneficial substances.

The stem cells may be obtained from any suitable source. In the case of human stem cells it should be noted, that the use of human embryonic stem cells may equivalently be substituted by the use of stem cells derived from other sources of precursor cells, i.e. by any appropriate alternative means known in the art. For example, Ernest Arenas et al. (Development, 2015, 142, 1918-1936 doi:10.1242/dev.097394) as well as Andrzej Swistowski et al. (Stem Cells 2010;28:1893–1904) describe ways to obtain midbrain dopaminergic neurons by differentiating cells that are not embryonic stem cells.

According to some embodiments, the differentiation can be induced e.g. by means of a surface structuring of the support surface or by electrical stimuli using the conductive properties of the optoelectric device. Thereby a specific device, such as an implantable device for the optically controlled release of a specific substance that is beneficial for treating a specific disease may be provided.

Further according to one embodiment of the optoelectric device the beneficial substance is a neurotransmitter, such as dopamine. Thereby, a device is provided that is useful for the treatment of neurological disorders that can be linked to a neurotransmitter deficiency, such as Parkinson's disease or epilepsy.

The optoelectric device may be an implantable device, and the optoelectric device may be particularly useful as an implantable device for the production, release, and delivery of therapeutic substances in a user. An implantable device with functional cells placed on a transparent carbon-based electrode applied to the outside of a leaky section of an optical fibre allows for directly stimulating the release of the beneficial substance from a cell culture by illumination through transparent regions of the conductive support surface, wherein the support surface simultaneously can be used for in-situ monitoring the release by electrochemical detection or measurement. In particular, an implantable device for the controlled release of neurotransmitters can be provided.

The implantable device may be adapted for cell replacement therapy in the brain of a mammal, such as a human being.

The photo-responsive biological components may be photosynthetic microorganisms, such as cyanobacteria, or algae. The optoelectric device with photosynthetic microorganisms arranged at the support surface is e.g. useful as an anode for a microbial photovoltaic system. Advantageous examples of photosynthetic microorganisms are cyanobacteria or algae. However, any biological component susceptible to the photosynthetic conversion of light input power, such as solar light, to electrical energy may be conceived for this function.

According to a third aspect, the object of the invention is achieved by a method of fabricating an optoelectric device as defined in the following, with the analogue advantages and effects as described above.

According to some embodiments, the method comprises the steps of: providing an optical waveguide configured for confining light propagating in a longitudinal direction thereof; providing a leaky section of the optical waveguide, wherein the

leaky section is configured for enhanced emission of light in a direction transverse or lateral to the longitudinal direction of the optical waveguide; coating the optical waveguide with an electrically conductive layer having a support surface for accommodating photo-responsive biological components and having transparent regions at least partially overlapping the leaky section for transmission of light to the photo-responsive biological components when accommodated at the support surface.

The step of coating may comprise pyrolysing a polymer layer to obtain an electrically conductive carbon layer with a surface adapted to act as the support surface, e.g. an immobilisation or growth support surface, configured to support photo-responsive components thereon, wherein the electrically conductive layer is at least partially transparent so as to allow for light from the leaky section of the optical waveguide to reach the support surface of the electrically conductive layer. The leaky section allows for an enhanced emission of light in a direction transverse or lateral to the longitudinal direction of the optical waveguide at least within one or more spectral bands, which may be referred to as one or more leaky bands.

Further according to one embodiment, the method further comprises the step of: patterning the polymer coating with a microscale pattern, prior to pyrolysing the polymer coating. The pattern may be applied e.g. using state of the art microscale pattern transfer techniques. Alternatively or in addition thereto, according to some embodiments, the method comprises steps of patterning the polymer coating with a nano-scale pattern, prior to pyrolysing the polymer coating.

Further according to one embodiment of the method the optical waveguide is an optical fibre.

Further according to one embodiment the method further comprises the step of: immobilising or cultivating a biological component of photo-responsive biological components on the surface. Preferably said photo-responsive biological components are responsive at least to radiation within the one or more leaky bands.

BRIEF DESCRIPTION OF THE DRAWINGS

Preferred embodiments of the invention will be described in more detail in connection with the appended drawings, which show in

Fig. 1A-D schematically steps of fabricating an optoelectric scaffold and an optoelectric device according to some embodiments of the invention, wherein Figs.1C and 1D show schematically embodiments of an optoelectric scaffold and an optoelectric device, respectively;

Fig. 2 schematically, a personalized treatment system comprising an implantable device according to one embodiment of the invention;

Fig. 3 schematically, an anode assembly for use in a bio-photovoltaic system;

Fig. 4 schematically, a bio-photovoltaic system with an anode assembly comprising optoelectrical devices according to some embodiments;

Fig. 5 a graph with cyclic voltammograms using an optical fibre with an electrically conductive carbon layer of pyrolysed polymer film;

Fig. 6 a graph with current traces generated when illuminating photo-responsive biological elements through a micro-structured electrically conductive carbon layer carrying the biological elements; and in

Fig. 7 a further graph with current traces generated when illuminating photo-responsive biological elements through a micro-structured electrically conductive carbon layer carrying the biological elements.

DETAILED DESCRIPTION

Referring to Figs.1A-D, steps of fabricating an optoelectric scaffold and an optoelectric device according to some embodiments of the invention are illustrated. In Fig.1A an optical waveguide 101 is provided in the form of an optical fibre. The optical fibre is configured for confining light for propagation in an axial direction Z

along a longitudinal direction of the fibre as indicated by the broken line. The optical waveguide 101 is further provided with a leaky section 102 allowing for an enhanced emission of light through a peripheral surface of the optical waveguide 101, in directions transverse or lateral of the optical waveguide 101, i.e. here in directions comprising a radial component perpendicular to the axial direction Z. The emission, or loss, of light from the leaky section 102 of the optical waveguide 101 is enhanced as e.g. compared to non-leaky sections 103 of the optical waveguide 101. In Fig.1B, at least the leaky section 102 of the optical waveguide 101 is coated with an organic polymer layer 104, e.g. a photosensitive resist as commonly used in microfabrication, such as an SU-8 based resist. The polymer layer 104 may optionally be provided with a nano- or microscale structure, and may further optionally be processed to form a three-dimensional structure (not shown). Techniques of micro-fabricating three-dimensional structures for subsequent pyrolysis in order to form immobilisation or growth support for biological components made of conductive carbon are e.g. disclosed in the co-pending European patent application EP 15186066. Fig.1C shows an embodiment of an optoelectric scaffold 100 with an electrically conductive carbon layer 105 arranged to at least overlap the leaky section 102 of the optical waveguide 101. The electrically conductive carbon layer 105 is here formed as a pyrolysed polymer layer, which is obtained after pyrolysis of the polymer coating 104 on the optical fibre 101. Fig.1D shows an embodiment of an optoelectric device 110, which has been obtained by cultivating a microbial culture of photo-responsive biological component 111 on an exposed surface of the electrically conductive carbon layer 105 acting as a growth support surface for the microorganisms 111. Light may be coupled into the optical waveguide 101 at a distal end thereof (not seen in Fig.1D), may then be guided along the longitudinal direction Z to the leaky section 102 of the optical waveguide with the electrically conductive carbon layer 105 thereon. The electrically conductive carbon layer 105 is at least partially transparent so as to allow for light from the leaky section 102 of the optical fibre to reach the growth support surface of the electrically conductive carbon layer 105, which carries the photo-sensitive biological components 111. In this way, a large amount of photo-sensitive biological components distributed over a relatively large surface area as compared to a cross-sectional footprint of the optoelectric device 110, or as compared to the device volume required, may thus be stimulated by a light input provided and controlled

remotely from the biological component. Also, multiple optoelectric devices 110 may easily be bundled without compromising the optical access to the microorganisms 111. At the same time, the electrically conductive carbon layer 105 can be used for monitoring the electrochemical environment and/or any activity of the biological components 111, such as monitoring optically stimulated exocytosis of certain substances. Monitoring may be performed by e.g. electrochemical measurements, such as voltammetry, using the optoelectric device 110 as an electrode of the monitoring set-up.

Fig. 2 illustrates schematically a personalized treatment system including an optoelectric device 200 configured for implantation in a user 99. The implantable device 200 comprises an optoelectric scaffold 100 with an optical fibre 101 having a leaky section 102. The leaky section 102 may comprise a microscale structuring providing an enhanced emission in transverse or lateral directions in a particular spectral range, such as a photonic band-gap structure as indicated in inset “A” in Fig.2. the leaky section 102 is at least partially covered by a conductive carbon electrode 105 made of a pyrolysed polymer film, which may e.g. comprise a three-dimensional microscale structuring, as indicated in inset “C” of Fig.2, acting as a functionalised scaffold for growing photo-responsive microorganisms 111 thereon, such as human neural stem cells. The three-dimensional structuring may improve cultivation, interconnectivity and/or electrical interaction between the biological component and the electrically conductive carbon layer. The micro-scale structuring may further be designed to promote differentiation of stem cells cultivated thereon. The photo-responsive biological components 111 may be adapted to produce a certain neurotransmitter, such as dopamine, and may be photo-responsive by promoting exocytosis of the neurotransmitter upon stimulation with a photonic signal as illustrated by the inset “B” in Fig.2. The photonic stimulation may be controlled by a control unit 201 of the personalized treatment system communicating with the implantable device 200, e.g. via a cabled or wire-less communication link 202. The control unit 201 may comprise a user interface displaying measurement results indicative of a disposition or condition of the user 99, and the personalized treatment of such condition may be in response to user input and/or controlled by programmed routines or algorithms for the automated or semi-automated treatment according to personalized parameters. Furthermore, the personalized treatment may be in

response to the measurement results indicative of a disposition or condition of the user 99 input to or received by the control unit 201. According to some embodiments, the implantable device 200 of the personalized treatment system may include measurement means adapted for providing measurements of indicative of a disposition or condition of the user 99, wherein the measurements may be provided as monitoring data in a regular or periodic manner and/or upon an external request, e.g. in reply to a user 99 initiated request and/or a programmed request from the control unit 201.

Figs. 3 and 4 show an alternative use of the optoelectric scaffold according to some embodiments of the invention in a bio-photovoltaic application. Fig. 3 shows schematically an anode arrangement 300, which is configured for use in a bio-photovoltaic system, such as the one illustrated in Fig.4. The anode 300 has a multitude of optoelectric devices 310 arranged in a bundle with a distal end arranged for receiving solar energy. Each of the optoelectric devices comprises an optoelectric scaffold made of an optical fibre with a long leaky section covered by a transparent electrically conductive carbon layer, preferably made of a pyrolysed polymer. The electrically conductive carbon layer carries on exposed surfaces thereof a culture of photo-synthetically active microorganisms, such as cyanobacteria or algae, as the photo-responsive microorganisms. The microorganisms are in electrical contact with the electrically conductive carbon layer, which in turn is electrically connectable to an external circuit to provide electrons to an electrical load (indicated as 330; not shown). The optoelectric anode 300 can thus collect light ($h\nu$) and guide that light to the inside of the anode, where it is gradually transferred in radial directions via leaky sections of the optical fibres to the photo-responsive microorganisms on the surface of the transparent conductive carbon coating. At the same time, the optoelectric anode 300 can, via the electrically conductive carbon layer, provide harvested electrons to a contact lead connectable to an external electric load 330.

Fig. 4 illustrates schematically a bio-photovoltaic system 400 useful for the conversion of light $h\nu$ into electrical power (e-) by means of photo-synthetically driven hydrolysis. The system comprises an anode 410 and a cathode 420

immersed in an aquatic medium, and electrically connected externally via an electric load 430.

The anode 410 is advantageously configured as the anode 300 described above with reference to Fig.3. Light (hν), typically sunlight, is coupled into an optical input end of the anode 410 and transferred to photo-synthetically active microorganisms 411 on growth surfaces of the electrically conductive carbon layers of the optoelectric scaffolds, here indicated as cyanobacteria (CYAN). In response to the light power received via the optical waveguide, the microorganisms 411 perform photosynthesis, inducing oxygen along with excess electrons. The excess electrons are collected by the anode 410, via external electrical circuitry the electrons are provided to the electric load 430, and further to the cathode 420, which donates electrons to reverse the hydrolysis reaction in an oxidation-reduction reaction with oxygen as the electron acceptor. The cathode reaction is typically catalysed by means of a metal such as platinum, either the cathode being a metal electrode itself or a metal deposited on the cathode. Alternatively, or additionally, enzymes are placed on the surface of the cathode to act as catalysts. Advantageously in the later case, the cathode 420 has a conductive carbon surface carrying an enzyme that catalyses an oxidation-reduction reaction, such as laccase (LAC as shown in Fig.4)) or bilirubin oxidase (BOx not shown in the figure). The conductive carbon substrate material of the cathode may be made of e.g. pyrolysed polymer, which further advantageously may be micro-structured to increase surface area and enhance electrical connectivity and external electron exchange between the enzyme and the conductive carbon substrate material.

Fig. 5 shows cyclic traces as obtained by voltammetry in ruthenium hexamine II/III using an optical fibre coated with a pyrolysed polymer film as an anode with sweep rates of 25 mV/s, 50 mV/s, and 100 mV/s, respectively.

Figs. 6 and 7 show by way of example different graphs with current traces obtained by illuminating photo-responsive biological elements accommodated on an electrically conductive layer and measuring the electrical response in a potentiostat set-up using the electrically conductive layer with the biological components thereon as a working electrode. In the present example, the photo-sensitive biological

components are thylakoid membranes, and the electrically conductive layer is a micro-structrured electrically conductive carbon layer. In the present example, the carbon layer has been produced by pyrolysing a micro-structured template of a precursor polymer layer carried on the front-side of a transparent quartz glass substrate. Here, the obtained pyrolysed carbon material is essentially opaque, but is made at least partially transparent by microscale openings produced by means of conventional photolithographic patterning of the precursor template prior to pyrolisation. A thylakoid membrane extract is distributed on the patterned surface of the pyrolysed carbon layer, allowed to gelify (by drying for 5 min), and then the carbon layer is electrically connected to the potentiostat to form the working electrode. The photo-responsive biological components are then illuminated “from behind”, i.e. through the electrically conductive layer accommodating the biological components by guiding light to the back side of the quartz substrate in the region of the patterned surface. The light will thus reach the photo-responsive systems on the supporting surface of the electrically conductive layer. In the present example, a soluble mediator, ruthenium III hexamine chloride, has been used to shuttle electrons between the thylakoids and the electrode surface.

The graphs shown in Figs. 6 and 7 show a clearly photo-induced current of the photo-responsive biological components in response to illumination through the conductive carrier layer accommodating the biological components.

The illuminating light was switched ON and OFF every 100 seconds. There is a clear current response when the light is turned on. When the light is turned off, the system stops producing current. The actual intensity of the response somewhat depends on the pattern coverage as indicated by the different traces 601-605 in Fig.6 and 701-705 in Fig.7. In all cases of the present example, the microscale patterning is a uniformly distributed arrangement of holes separated from each other by continuous lines of the conductive material. The holes provide optical access through the electrically conductive layer for illuminating the photo-responsive biological components thereon, and the continuous lines of the conductive material form a network of electrical leads for the collection of electrical current generated in response to the illumination.

Note that the pyrolysed carbon material forming the electrically conductive layer of the present example is actually opaque, but has successfully been made sufficiently transparent by providing a microscale pattern of openings, yet ensuring an efficient current collection. The example of Figs. 6 and 7 thus also illustrates that the invention can even be exercised using an otherwise opaque electrically conductive layer as a support for accommodating the photo-responsive biological components, as long as the opaque layer comprises transparent regions, e.g. provided in the form of a pattern with microscale openings.

Table 1 summarizes the particular geometry parameters of the patterns used for producing the traces 601-605 in Fig.6. and Table 2 summarizes the corresponding geometry parameters for traces 701-705 in Fig.7. The holes are square shaped and hole sizes are given as the side length of the squares in micrometres. Hole-coverage is the fraction in percent of the patterned area covered by holes. Carbon coverage is the complementary fraction in percent of the patterned area covered by the electrically conductive material made of SU8-derived pyrolysed carbon. The electrochemical measurements were performed on samples with an active patterned area of about 8mm in diameter as delimited by an O-ring.

Table 1

Trace	hole size / µm	hole coverage / %	carbon coverage / %
601	20	40	60
602	50	40	60
603	100	40	60
604	200	40	60
605	400	40	60

Table 2

Trace	hole size / µm	hole coverage / %	carbon coverage / %
701	Full hole	100	0
702	100	20	80
703	100	40	60
704	100	60	40
705	Full C	0	100

Generally speaking, microscale openings in an otherwise opaque conductive layer can advantageously be used as one means of providing sufficient transparency for illuminating the photo-responsive biological elements from behind, i.e. through the conductive layer acting as a support.

While the actual shape of the openings is subordinate, the scale of the microstructure plays a role. For a given fraction of uncovered area (40% in Fig.6), a microstructure with smaller dimensions of the openings is apparently better for an efficient current collection. Also, as evident from Fig.7, for given hole dimensions (100µm square holes in Fig.7) an increased fraction of opening apparently increases the photo-induced response as more and more light reaches the photo-responsive biological components as long as an efficient current collection can be performed. An upper limit is illustrated in the limit of “full hole coverage” in trace 701, i.e. where no material of the electrically conductive material remains in the patterned area for collecting current. The remaining photo-response is here carried through the photo-responsive biological components, i.e. here through the applied layer of gelified thylakoid membrane extract. The reference measurement (trace 705) with full coverage of the electrically conductive material shows that the material used here, i.e. the pyrolysed carbon layer, is apparently opaque. No significant photo-response is detected in this case (trace 705).

Advantageously the openings have a cross-sectional dimension of less than and up to 500µm, less than and up to 200µm, less than and up to 100µm, less than or up to 50µm, or less than and up to 20µm. Further advantageously, the hole coverage is at least 10%, at least 20%, at least 40%, or at least 60%. Further advantageously, the hole coverage is less than and up to 90%, or less than and up to 80%.

CLAIMS

1. Optoelectric scaffold for accommodating photo-responsive biological components, the scaffold comprising an optical waveguide configured for confining light propagating in a longitudinal direction thereof, the optical waveguide comprising:

   at least one leaky section configured for supporting leaky modes with an enhanced emission of light in a direction transverse or lateral to the longitudinal direction of the optical waveguide as compared to guided or confined modes;

   and

   a biocompatible electrically conductive layer arranged on an outer surface of the optical waveguide, the electrically conductive layer having

   - a support surface configured for accommodating photo-responsive biological components, and
   - transparent regions at least partially overlapping the at least one leaky section for transmission of light to photo-responsive biological components when accommodated at the support surface.

2. Optoelectric scaffold according to claim 1, wherein the electrically conductive layer comprises an electrically conductive carbon layer.

3. Optoelectric scaffold according to any of the preceding claims, wherein the electrically conductive layer is a pyrolysed polymer film.

4. Optoelectric scaffold according to any of the preceding claims, wherein the optical waveguide is an optical fibre.

5. Optoelectric scaffold according to any of the preceding claims, wherein the optical waveguide comprises photonic crystals.

6. Optoelectric device comprising an optoelectric scaffold according to any of the preceding claims, the device further comprising photo-responsive biological

components accommodated at the support surface, wherein the photo-responsive biological components are in electrical contact with the electrically conductive layer, and wherein the photo-responsive biological components are arranged to receive light from the optical waveguide at the at least one leaky section, through the transparent regions of the electrically conductive material.

7. Optoelectric device according to claim 6, wherein the photo-responsive biological components are adapted for the photo-stimulated release of a substance beneficial for the treatment of a disease.

8. Optoelectric device according to any one of claims 6-7, wherein the photo-responsive biological components comprise stem cells.

9. Optoelectric device according to claim 8, wherein the stem cells are not human embryonic stem cells.

10. Optoelectric device according to any one of claims 7-9, wherein the beneficial substance comprises a neurotransmitter, or therapeutic factors, for neuromodulation, neuroprotection and/or neuroregeneration.

11. Optoelectric device according to any one of claims 7-10, wherein the beneficial substance comprises dopamine.

12. Optoelectric device according to claim 6, wherein the photo-responsive biological components comprise photosynthetic microorganisms.

13. Optoelectric device according to any one of claim 6 or claim 12, wherein the photo-responsive biological components comprise cyanobacteria or algae, or photo responsive components or organelles of microorganisms.

14. Optoelectric device according to any one of claim 6, claim 12, or claim 13, wherein the photo-responsive biological components comprise proteins, bacteriorhodopsin, thylakoid membranes, or chloroplasts.

15. Optoelectric device according to any one of claims 6-14, wherein the optoelectric device is an implantable device.

16. A personalized treatment system comprising an optoelectric device according to claim 15, and a control unit adapted to communicate with the optoelectric device.

17. Method of fabricating an optoelectric device, the method comprising the steps of

- providing an optical waveguide configured for confining light propagating in a longitudinal direction thereof,
- providing a leaky section of the optical waveguide, wherein the leaky section is configured for supporting leaky modes with an enhanced emission of light in a direction lateral to the longitudinal direction of the optical waveguide as compared to guided or confined modes;
- coating the optical waveguide with a biocompatible electrically conductive layer, the electrically conductive layer having a support surface for accommodating photo-responsive biological components and having transparent regions at least partially overlapping the leaky section for transmission of light to photo-responsive biological components when accommodated at the support surface.

18. Method according to claim 17, wherein the electrically conductive layer comprises an electrically conductive carbon layer.

19. Method according to claim 18, wherein the step of coating comprises

- pyrolysing a polymer layer to obtain the electrically conductive carbon layer with a surface adapted to act as the support surface.

20. Method according to claim 19, further comprising the step of

- patterning the polymer layer with a microscale pattern, prior to pyrolysing the polymer layer.

21. Method according to any one of claims 17-20, further comprising the step of
    - immobilising or cultivating photo-responsive biological components at the support surface.

22. Method according to claim 21, wherein the photo-responsive biological components are adapted for the photo-stimulated release of a substance beneficial for the treatment of a disease.

23. Method according to any one of claims 21-22, wherein the photo-responsive biological components comprise stem cells.

24. Method according to claim 23, wherein the stem cells are not human embryonic stem cells.

25. Method according to any one of claims 22-24, wherein the beneficial substance comprises a neurotransmitter, or therapeutic factors, for neuromodulation, neuroprotection and/or neuroregeneration.

26. Method according to any one of claims 22-25, wherein the beneficial substance comprises dopamine.

27. Method according to claim 21, wherein the photo-responsive biological components comprise photosynthetic microorganisms.

28. Method according to any one of claim 21 or claim 27, wherein the photo-responsive biological components comprise cyanobacteria or algae.

29. Method according to any one of claim 21, claim 27, or claim 28, wherein the photo-responsive biological components comprise cyanobacteria or algae, or photo responsive components or organelles of microorganisms.

30. Method according to any one of claim 21, claim 27, claim 28, or claim 29, wherein the photo-responsive biological components comprise proteins, bacteriorhodopsin, thylakoid membranes, or chloroplasts.

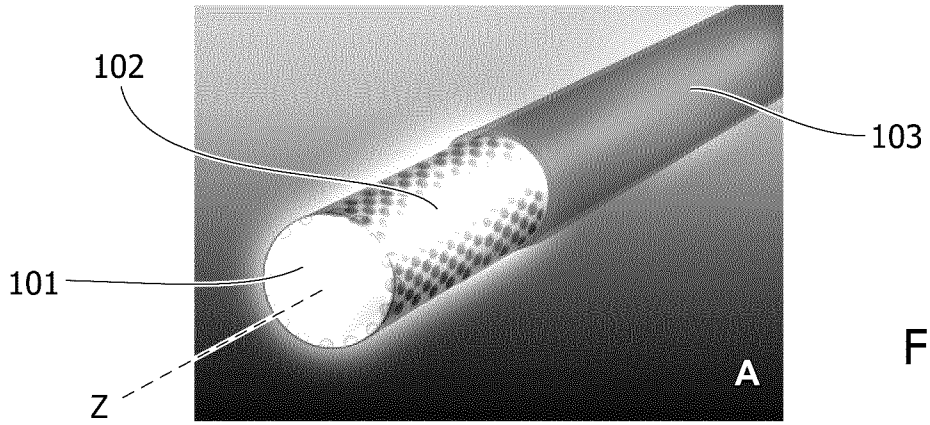


Fig. 1A

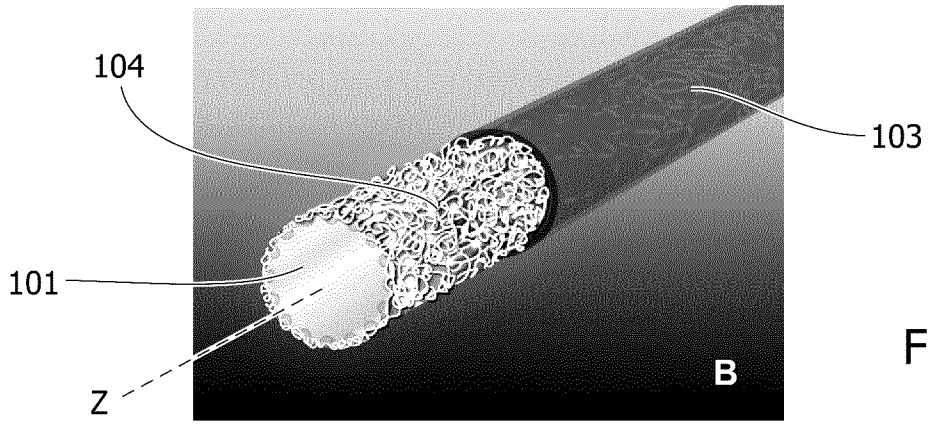


Fig. 1B

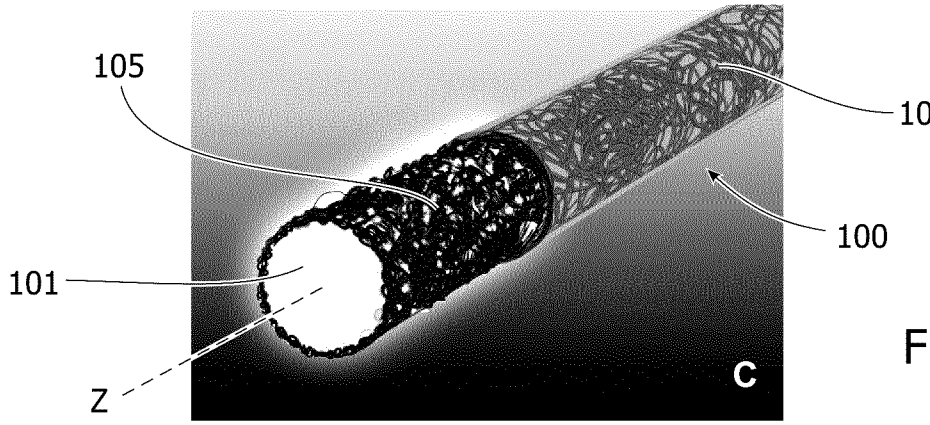


Fig. 1C

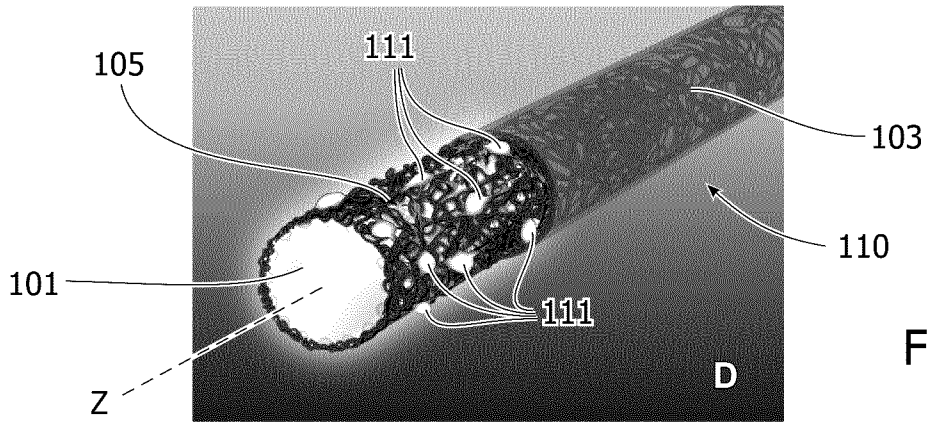
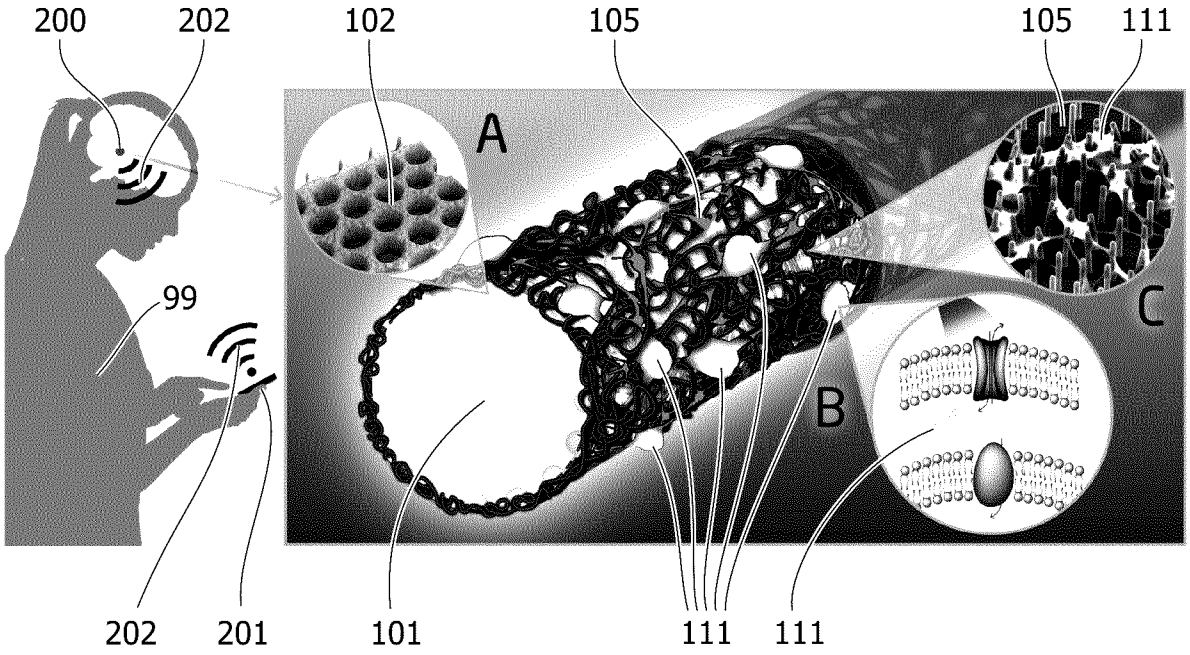


Fig. 1D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202
102
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105
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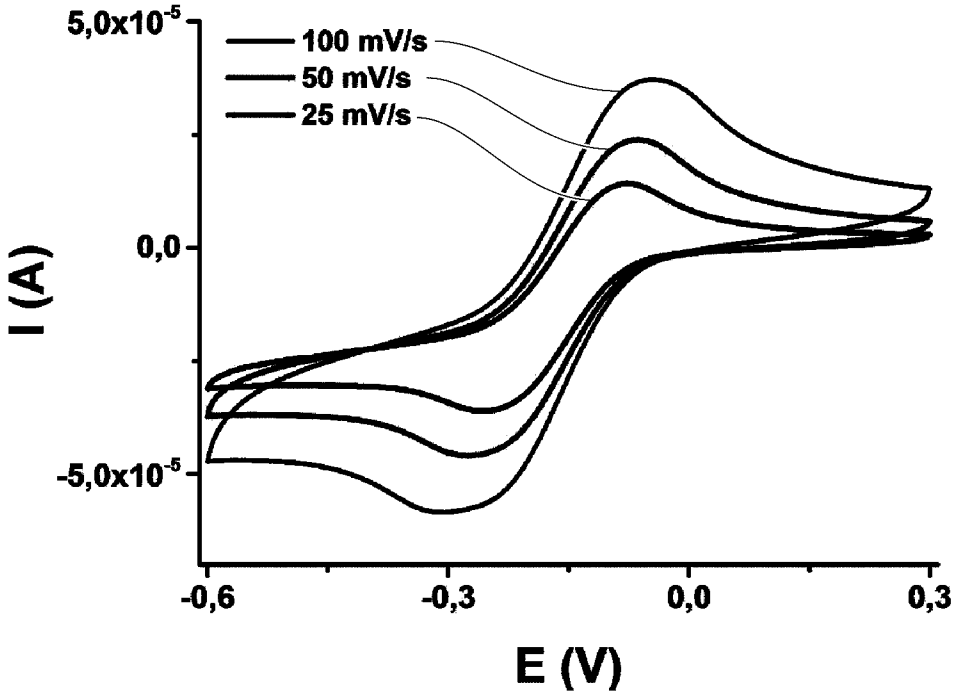
A
99
B
C
202
201
101
111
111

Fig. 2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100 mV/s
50 mV/s
25 mV/s
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0,3
E (V)

Fig. 5

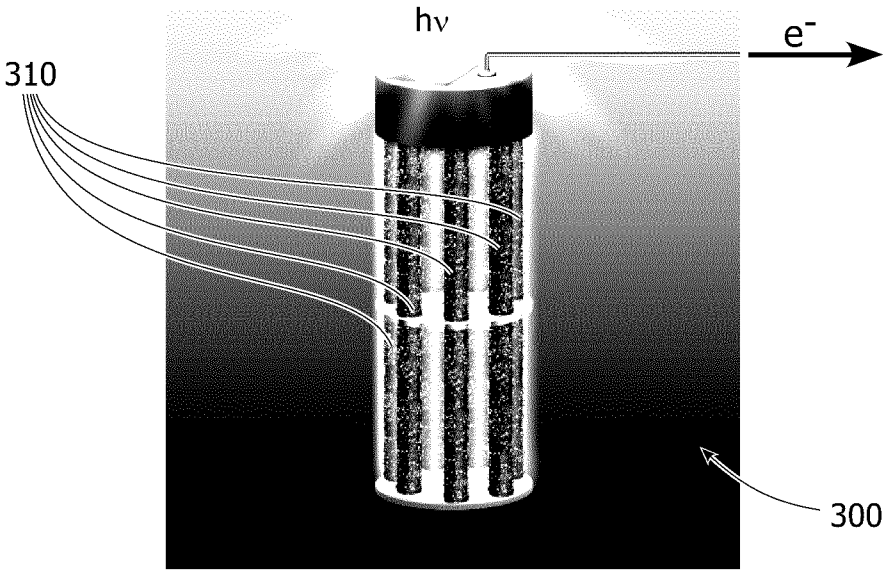
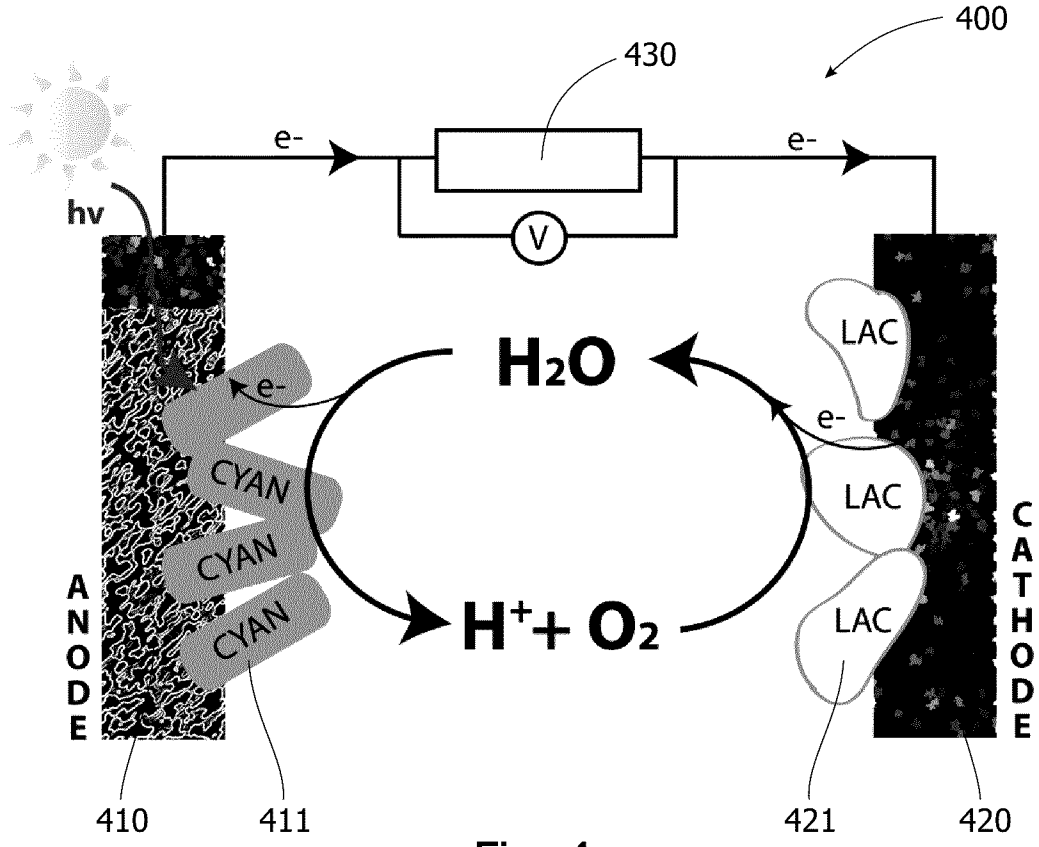

hν
e-
310
300

Fig. 3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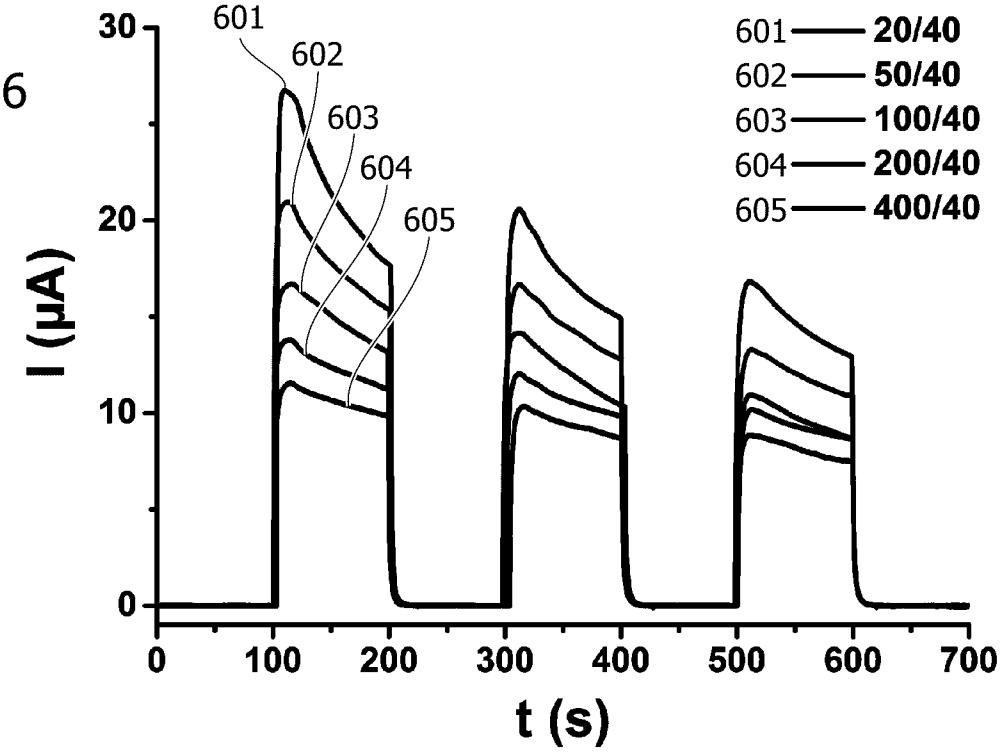
430
e-
e-
V
hv
H2O
e-
e-
CYAN
CYAN
CYAN
LAC
LAC
LAC
H+ + O2
ANODE
CATHODE
410
411
421
420

Fig. 4

Fig. 6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602
603
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605
601 — 20/40
602 — 50/40
603 — 100/40
604 — 200/40
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30
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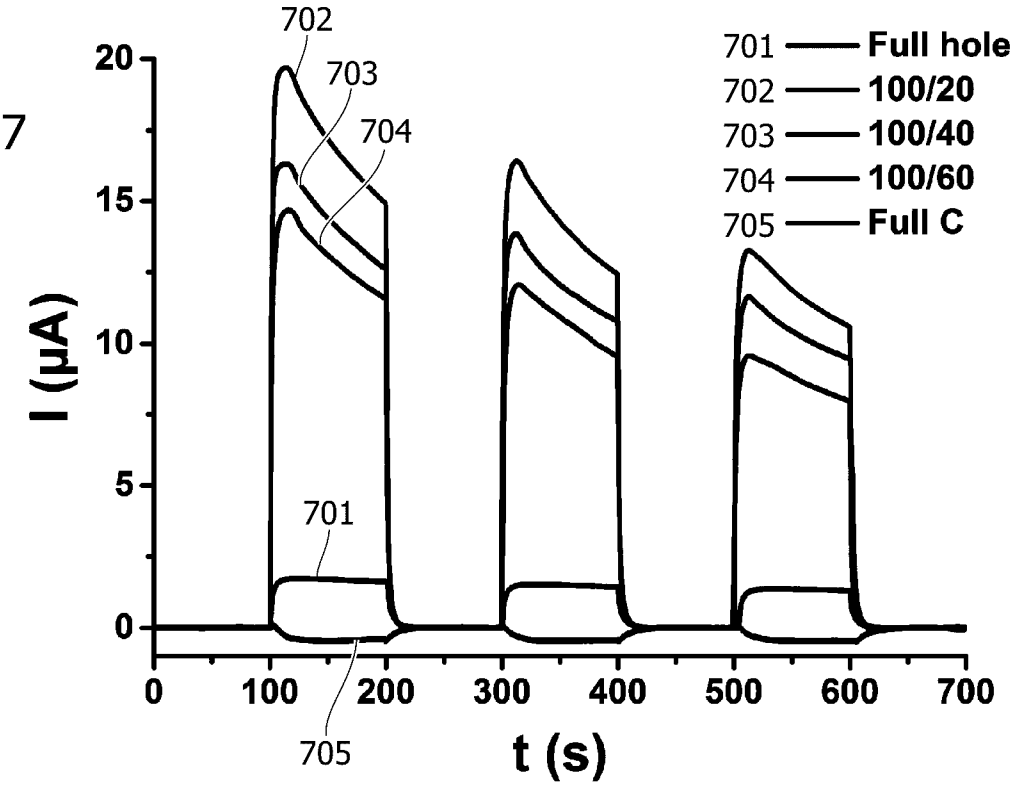
400
500
600
700

Fig. 7


702
703
704
701
705
701 — Full hole
702 — 100/20
703 — 100/40
704 — 100/60
705 — Full C
I (μA)
t (s)
0
5
10
15
20
0
100
200
300
400
500
600
700

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2017/066157

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12Q1/00 G01N33/50 G01N33/543
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	L. AMATO ET AL.: "Pyrolysed 3D-Carbon Scaffolds Induce Spontaneous Differentiation of Human Neural Stem Cells and Facilitate Real-Time Dopamine Detection", ADVANCED FUNCTIONAL MATERIALS, vol. 24, no. 44, 1 November 2014 (2014-11-01), pages 7042-7052, XP055324926, Weinheim ISSN: 1616-301X, DOI: 10.1002/adfm.201400812 cited in the application the whole document	1-30
A	WO 2013/171520 A1 (ISIS INNOVATION [GB]) 21 November 2013 (2013-11-21) abstract	1-30

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 July 2017	08/08/2017

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Van Bohemen, Charles

2

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	H.H. LIU & H.C. CHANG: "Leaky Surface Plasmon Polariton Modes at an Interface Between Metal and Uniaxially Anisotropic Materials", PHOTONICS JOURNAL (INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS), vol. 5, no. 6, 1 December 2013 (2013-12-01), page 4800806, XP011531787, New York, NY, USA DOI: 10.1109/JPHOT.2013.2288298 abstract -----	1-30

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/066157

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2013171520 A1	21-11-2013	EP 2850669 A1	25-03-2015
		EP 3010054 A1	20-04-2016
		ES 2566914 T3	18-04-2016
		US 2015129034 A1	14-05-2015
		WO 2013171520 A1	21-11-2013